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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,204	01/18/2005	Frank Brady	PH0249	3678
36335	7590	09/26/2007	EXAMINER	
GE HEALTHCARE, INC. IP DEPARTMENT 101 CARNEGIE CENTER PRINCETON, NJ 08540-6231			NAGUBANDI, LALITHA	
			ART UNIT	PAPER NUMBER
			1621	
			MAIL DATE	DELIVERY MODE
			09/26/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/522,204	Applicant(s) BRADY ET AL.	
	Examiner Lalitha Nagubandi	Art Unit 1621	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 July 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 8 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4 is/are allowed.
- 6) ☒ Claim(s) 1-3,5 and 6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

***Detailed Action***

***Status of the Claims***

Claims 1-8 are pending. Claims 1-6 are considered in this office action.

***Response to Argument***

Applicants' arguments filed on July 19<sup>th</sup> 2007, with respect to the previous office action, have been fully considered. The rejection under 35 U.S.C. § 103 of claims 1-6 has been withdrawn in view of the remarks made by the applicants. Upon further review of the claims the following rejection is being made.

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

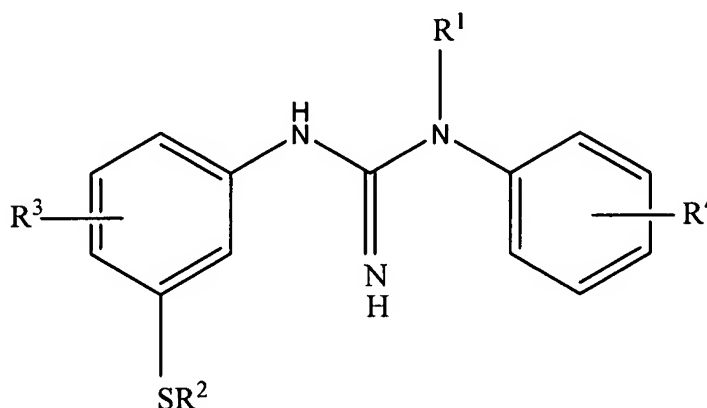
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1- 3, 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hu et al (J. Med. Chem. 1997, 40, 4281-4289) and in view of Shiue et al (Nuclear Medicine and Biology, vol. 24, pp. 145 – 150, 1997).

Applicants claim a compound of **Formula (I)**:



Wherein, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and R<sup>4</sup> are as defined. The compounds further contain R<sup>1</sup> as <sup>11</sup>C- alkyl or -CH<sub>2</sub> <sup>18</sup>F, to -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub> <sup>18</sup>F. The instant compounds are claimed to be useful in diagnostic studies like Positron Emission Tomography (PET).

**Determination of Scope and content of the Prior Art (MPEP § 2141.01)**

Hu et al teach substituted N-methyl guanidine analogs ( see table 4. page 4285, J. Med. Chem. 1997, 40, 4281-4289) where the N-Me hydrogens are radiolabeled. Further,

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Hu teaches the binding of various N-methyl guanidine analogs to the N-methyl-D-aspartate (NMDA) glutamate receptor ion-channel site.

Shieu et al teach C-11 labeled compounds and PET studies (see scheme 1, page 146, Nuclear Medicine and Biology, vol. 24, pp. 145 – 150, 1997).

**Ascertainment of the difference between the Prior Art and Claims (MPEP §2141.02)**

The difference between the instant compounds and Hu et al is that some of the instant compounds requires tracer element like  $^{11}\text{C}$  at the N'-Me position of the guanidine moiety.

Shieu et al teaches Carbon-11, N-Me compounds. However, the radiolabelled compounds are ketamine and its enantiomers.

**Finding of prima facie obviousness – rational and motivation (MPEP § 142-2143)**

One of ordinary skill in the art would be motivated to prepare the instant compounds by modifying the C-11, N-Me compounds as taught by Shieu et al in the teachings of Hu and investigate the novel compounds in binding studies.

Substitutions around the core structure, since the diphenyl substituted guanidine core is already known in the prior art. Introduction of a tracer element like  $^{11}\text{C}$  at the N-Me position of the guanidine or at other substituents would have been obvious to one skilled in the radiosynthetic field. The examiner contends that the combination of references is proper and an ordinary artisan would have had a reasonable expectation

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of success at the time of the instant invention to arrive at the instant imaging compounds and hence it is prima facie.

***Allowable Subject Matter***

*The elected species of **Example 2**, (N-(2-chloro-5-(methylthio)phenyl)-N'-(3-methylthio)phenyl)N'-[<sup>18</sup>F]fluoromethylguanidine was searched and found to be allowable.*

Claim 4 was found allowable

The following is a statement of reasons for the indication of allowable subject matter:

The instant compounds of formula (Ic) as embodied in **claim 4**, where R<sup>3c</sup> is radioiodine when S on the phenyl ring attached to the NH is substituted as claimed in the instant invention, render unobvious to one skilled in the art as the closest prior art of record does not teach or suggest the instant compounds of **claim 4**.

***Conclusion***

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lalitha Nagubandi whose telephone number is 571 272 7996.

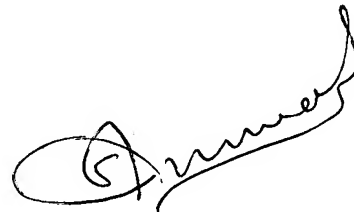
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The examiner can normally be reached on 6.30 am to 3.30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne, Eyler can be reached on 571 272 0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0871.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lalitha Nagubandi  
Patent Examiner  
Technology Center 1600

September 24<sup>th</sup>, 2007.

A handwritten signature in black ink, appearing to read 'Shailendra Kumar', with a large, stylized initial 'S'.

Shailendra Kumar  
Primary Patent Examiner  
Technology Center 1600